claims and title of the application; and 3) A replacement Sequence Listing provided in electronic copy on diskette and a paper copy of the Sequence Listing, along with a Response requesting entry thereof.

Reconsideration of this application and pending claims in view of the amendments and discussion below is respectfully requested.

IN THE SPECIFICATION

Please enter the numbered amendments to the specification below, the amendments of which are provided in Appendix I except the first one.

1. At page 1, lines 1-2, please delete the title "METHODS AND COMPOSITIONS USEFUL FOR INHIBITION OF ANGIOGENESIS" and replace with "INHIBITION OF ANGIOGENESIS IN DISEASE STATES WITH AN ANTI-$\alpha_v\beta_3$ MONOCLONAL ANTIBODY".

2. At page 1, line 23, continuing to page 2, line 1, please delete the paragraph and replace with the amended paragraph:

The vitronectin receptor, named for its original characteristic of preferential binding to vitronectin, is now known to refer to three different integrins, designated $\alpha_v\beta_1$ $\alpha_v\beta_3$ and $\alpha_v\beta_5$. Horton, Int. J. Exp. Pathol., 71:741-759 (1990). $\alpha_v\beta_1$ binds fibronectin and vitronectin. $\alpha_v\beta_3$ binds a large variety of ligands, including fibrin, fibrinogen, laminin, thrombospondin, vitronectin, von Willebrand's factor, osteopontin and bone sialoprotein I. $\alpha_v\beta_5$ binds vitronectin. The specific cell adhesion roles these three integrins play in the many cellular interaction in tissues is still under investigation, but it is clear that there are different integrins with different biological functions.

3. At page 4, line 24, continuing to page 25, line 7, please delete the paragraph and replace with the amended paragraph:

Inhibition of cell adhesion in vitro using monoclonal antibodies immunospecific for various integrin α or β subunits have implicated $\alpha_v\beta_3$ in cell adhesion of a variety of cell types including microvascular endothelial cells. Davis et al., J. Cell. Biol., 51:206-218 (1993). In addition, Nicosia et al., Am. J. Pathol., 138:829-833 (1991), described the use of the RGD peptide GRGDS (SEQ ID NO 15) to in vitro inhibit the formulation of "microvessels" from rat aorta cultured in collagen gel. However, the inhibition of formulation of "microvessels" in vitro in collagen gel cultures is not a model for inhibition of angiogenesis in a tissue because it is not shown that the microvessel structures are the same as capillary sprouts or that the formulation of the microvessel in collagen gel culture is the same as neo-vascular growth into an intact tissue, such as arthritic tissue, tumor tissue or disease tissue where inhibition of angiogenesis is desirable.

4. At page 11, lines 14-19, please delete the paragraph and replace with the amended paragraph:

Cyclic peptide: is derived from a corresponding linear peptide and; refers to a peptide in which no free N- or C-termini exist and; and of which the corresponding linear peptide's N-termini forms an amide bond to the C-terminal carboxylate of the said corresponding linear peptide.

5. At page 27, lines 16-18, please delete the paragraph and replace with the amended paragraph:

Labels, solid matrices and carriers that can be used with the polypeptides of this invention are described herein below.

6. At page 39, line 17, continuing to page 40, line 1, please delete the paragraph and replace with the amended paragraph:

Two grams (g) of BOC-Gly-D-Arg-Gly-Asp-Phe-Val-OMe (SEQ ID NO 1) were first dissolved in 60 milliliters (ml) of methanol to which was added 1.5 ml of 2 N sodium hydroxide solution to form an admixture. The admixture was then stirred for 3 hours at 20 degrees C (20C). After evaporation, the residue was taken up in water, acidified to pH 3 with diluted HCl and extracted with ethyl acetate. The extract was dried over Na_2SO_4, evaporated again and the resultant BOC-Gly-D-Arg-Gly-Asp-Phe-Val-OH (SEQ ID NO 2) was stirred at 20C for 2 hours with 20 ml of 2 N HCl in dioxane. The resultant admixture was evaporated to obtain H-Gly-D-Arg-Gly-Asp-Phe-Val-OH (SEQ ID NO 3) that was subsequently dissolved in a mixture of 1800 ml of dichloromethane and 200 ml of dimethylformamide (DMF) followed by cooling to 0C. Thereafter, 0.5 g of dicyclohexylcarbodiimide (DCCI), 0.3 g of 1-hydroxybenzotriazole (HOBt) and 0.23 ml of N-methylmorpholine were added successively with stirring.

7. At page 41, lines 10-21, please delete the paragraph and replace with the amended paragraph:

The monoclonal antibody LM609 secreted by hybridoma ATCC HB 9537 was produced using standard hybridoma methods by immunization with isolated $\alpha_v\beta_3$ adsorbed onto SEPHAROSE-lentil lectin beads. The $\alpha_v\beta_3$ had been isolated from human melanoma cells designated M21, and antibody was produced as described by Cheresh et al., J. Biol. Chem., 262:17703-17711 (1987). M21 cells were provided by Dr. D.L. Morton (University of California at Los Angeles, CA) and grown in suspension cultures in RPMI 1640 culture medium containing 2 mM L-glutamine, 50 mg/ml gentamicin sulfate and 10 % fetal calf serum.

8. At page 49, lines 15-29, please delete the paragraph and replace with the amended paragraph:

To view the tissue distribution of integrin receptors present in CAM tissues, 6 micron (um) frozen sections of both tumor tissue and chick embryo CAM tissues were

fixed in acetone for 30 seconds and stained by immunofluorescence with 10 micrograms/milliliter (ug/ml) mAb CSAT, a monoclonal antibody specific for the β_1 integrin subunit as described by Buck et al., J. Cell Biol., 107:2351 (1988) and thus used for controls, or LM609 as prepared in Example 2. Primary staining was followed by staining with a 1:250 dilution of goat anti-mouse rhodamine labeled secondary antibody (Tango) to allow for the detection of the primary immunoreaction product. The sections were then analyzed with a Zeiss immunofluorescence compound microscope.

9. At page 56, lines 5-15, please delete the paragraph and replace with the amended paragraph:

CAM assays were also performed with the synthetic peptides of this invention to determine the effect of cyclic and linearized peptides on growth factor induced angiogenesis. The peptides were prepared as described in Example 1 and 80 ug of peptide was presented in a total volume of 25 ul of sterile HBSS. The peptide solution was applied to the CAM preparation immediately and then again at 24 and 48 hrs. At 72 hours the filter paper and surrounding CAM tissue was dissected and viewed as described above.

IN THE CLAIMS

Please cancel claims 17-170 without prejudice.

Please add new claims 171-286 as follows:

--171. (New) A method for inhibiting bladder, breast, colon or lung tumor tissue growth in a human in need thereof comprising administering to said tumor a composition comprising an angiogenesis-inhibiting amount of a monoclonal antibody immunospecific for $\alpha_v\beta_3$.